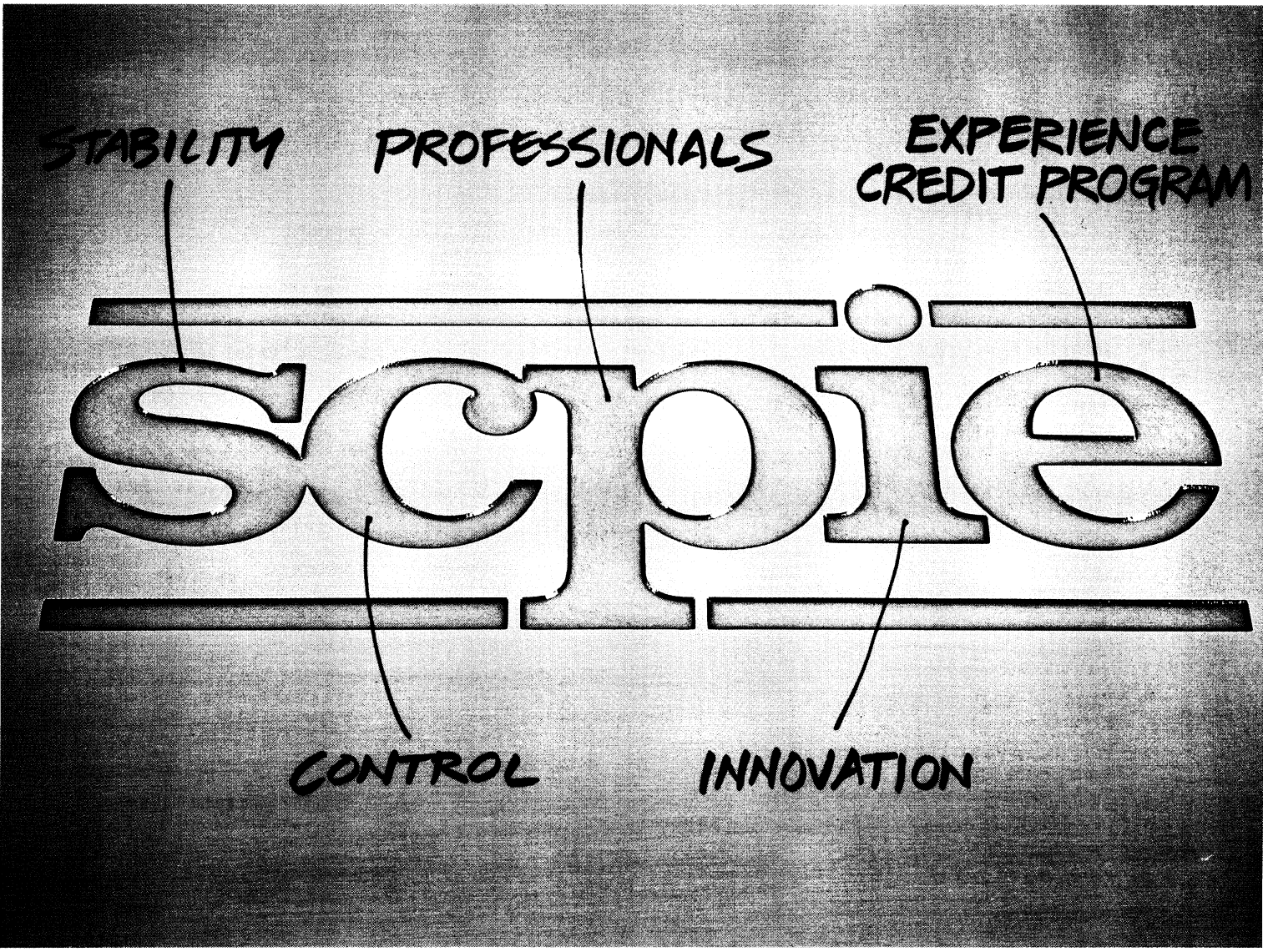

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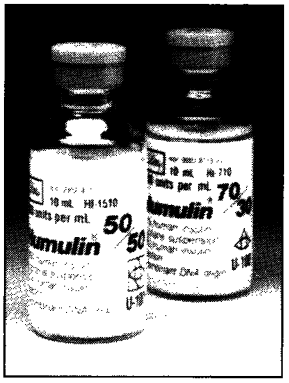

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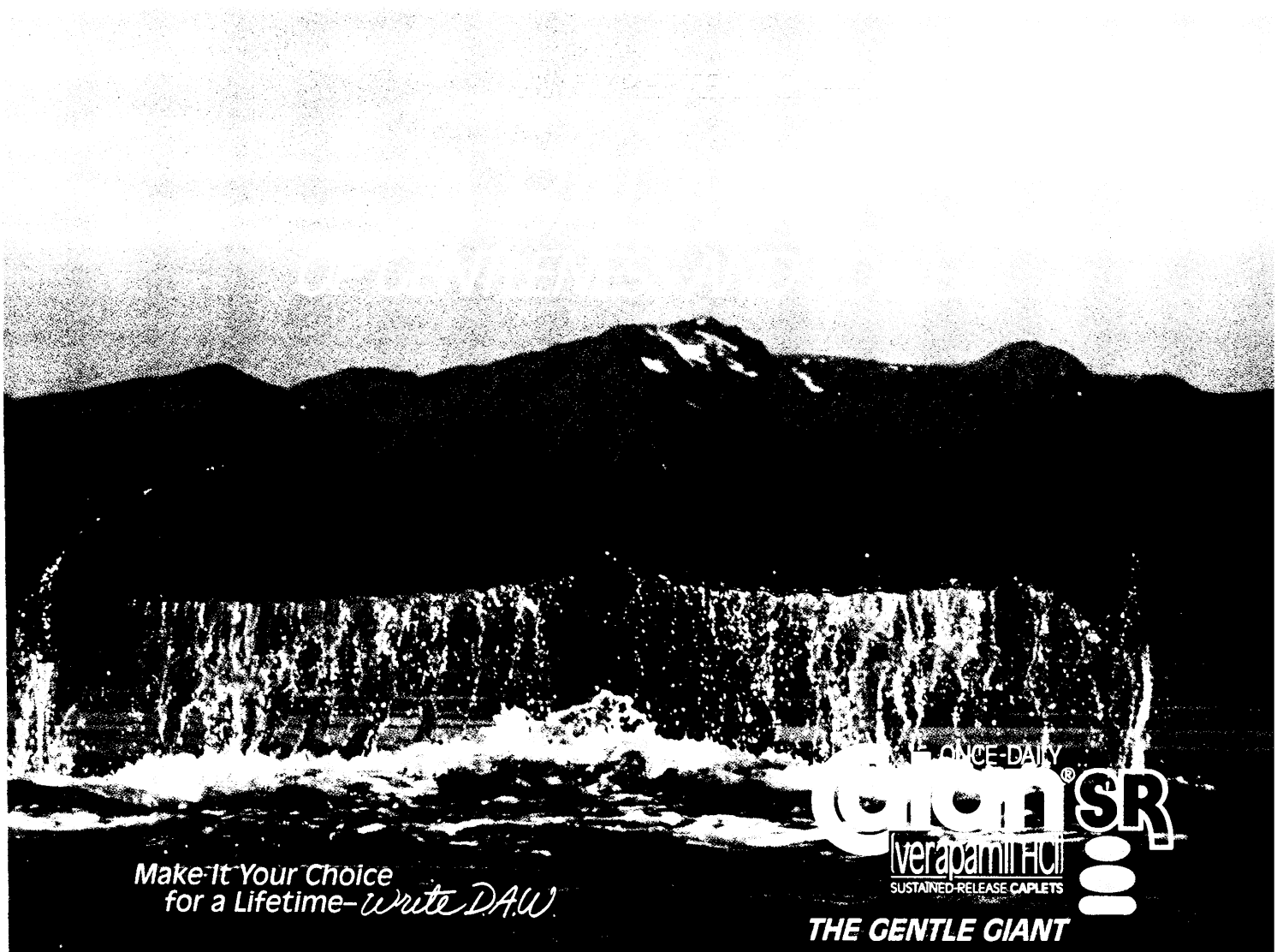

The recommended starting dosage for Calan SR is 180 mg once daily. Dose titration will be required in some patients to achieve blood pressure control. A lower starting dosage of 120 mg/day may be warranted in some patients (eg, the elderly, patients of small stature). Dosages above 240 mg daily should be administered in divided doses. Calan SR should be administered with food. Constipation, which is easily managed in most patients, is the most commonly reported side effect of Calan SR.

BRIEF SUMMARY

Contraindications: Severe LV dysfunction (see *Warnings*), hypotension (systolic pressure < 90 mm Hg) or cardiogenic shock, sick sinus syndrome (if no pacemaker is present), 2nd- or 3rd-degree AV block (if no pacemaker is present), atrial flutter/fibrillation with an accessory bypass tract (eg, WPW or LGL syndromes), hypersensitivity to verapamil.

Warnings: Verapamil should be avoided in patients with severe LV dysfunction (eg, ejection fraction < 30%) or moderate to severe symptoms of cardiac failure and in patients with any degree of ventricular dysfunction if they are receiving a beta-blocker. Control milder heart failure with optimum digitalization and/or diuretics before Calan SR is used. Verapamil may occasionally produce hypotension. Elevations of liver enzymes have been reported. Several cases have been demonstrated to be produced by verapamil. Periodic monitoring of liver function in patients on verapamil is prudent. Some patients with paroxysmal and/or chronic atrial flutter/fibrillation and an accessory AV pathway (eg, WPW or LGL syndromes) have developed an increased antegrade conduction across the accessory pathway bypassing the AV node, producing a very rapid ventricular response or ventricular fibrillation after receiving I.V. verapamil (or digitalis). Because of this risk, oral verapamil is contraindicated in such patients. AV block may occur (2nd- and 3rd-degree, 0.8%). Development of marked 1st-degree block or progression to 2nd- or 3rd-degree block requires reduction in dosage or, rarely, discontinuation and institution of appropriate therapy. Sinus bradycardia, 2nd-degree AV block, sinus arrest, pulmonary edema and/or severe hypotension were seen in some critically ill patients with hypertrophic cardiomyopathy who were treated with verapamil.

Precautions: Verapamil should be given cautiously to patients with impaired hepatic function (in severe dysfunction use about 30% of the normal dose) or impaired renal function, and patients should be monitored for abnormal prolongation of the PR interval or other signs of overdosage. Verapamil may decrease neuromuscular transmission in patients with Duchenne's muscular dystrophy and may prolong recovery from the neuromuscular blocking agent vecuronium. It may be necessary to decrease verapamil dosage in patients with attenuated neuromuscular transmission. Combined therapy with beta-adrenergic blockers and verapamil may result in additive negative effects on heart rate, atrioventricular conduction and/or cardiac contractility; there have been reports of excessive bradycardia and AV block, including complete heart block. The risks of such combined therapy may outweigh the benefits. The combination should be used only with caution and close monitoring. Decreased metoprolol and propranolol clearance may occur when either drug is administered concomitantly with verapamil. A variable effect has been seen with combined use of atenolol. Chronic verapamil treatment can increase serum digoxin levels by 50% to 75% during the first week of therapy, which can result in digitalis toxicity. In patients with hepatic cirrhosis, verapamil may reduce total body clearance and extrarenal clearance of digitoxin. The digoxin dose should be reduced when verapamil is given, and the patient carefully monitored. Verapamil will usually have an additive effect in patients receiving blood-pressure-lowering agents. Disopyramide should not be given within 48 hours before or 24 hours after verapamil administration. Concomitant use of flecainide and verapamil may have additive effects on myocardial contractility, AV conduction, and repolarization. Combined verapamil and quinidine therapy in patients with hypertrophic cardiomyopathy should be avoided, since significant hypotension may result. Concomitant use of lithium and verapamil may result in an increased sensitivity to lithium (neurotoxicity), with either no change or an increase in serum lithium levels; however, it may also result in a lowering of serum lithium levels. Patients receiving both drugs must be monitored carefully. Verapamil may increase carbamazepine concentrations during combined use. Rifampin may reduce verapamil bioavailability. Phenobarbital may increase verapamil clearance. Verapamil may increase serum levels of cyclosporin. Verapamil may inhibit the clearance and increase the plasma levels of theophylline. Concomitant use of inhalation anesthetics and calcium antagonists needs careful titration to avoid excessive cardiovascular depression. Verapamil may potentiate the activity of neuromuscular blocking agents (curare-like and depolarizing); dosage reduction may be required. There was no evidence of a carcinogenic potential of verapamil administered to rats for 2 years. A study in rats did not suggest a tumorigenic potential, and verapamil was not mutagenic in the Ames test. Pregnancy Category C. There are no adequate and well-controlled studies in pregnant women. This drug should be used during pregnancy, labor, and delivery only if clearly needed. Verapamil is excreted in breast milk; therefore, nursing should be discontinued during verapamil use.

Adverse Reactions: Constipation (7.3%), dizziness (3.3%), nausea (2.7%), hypotension (2.5%), headache (2.2%), edema (1.9%), CHF, pulmonary edema (1.8%), fatigue (1.7%), dyspnea (1.4%), bradycardia: HR < 50/min (1.4%), AV block: total 1°,2°,3° (1.2%), 2° and 3° (0.8%), rash (1.2%), flushing (0.6%), elevated liver enzymes, reversible non-obstructive paralytic ileus. The following reactions, reported in 1.0% or less of patients, occurred under conditions where a causal relationship is uncertain: angina pectoris, atrioventricular dissociation, chest pain, claudication, myocardial infarction, palpitations, purpura (vasculitis), syncope, diarrhea, dry mouth, gastrointestinal distress, gingival hyperplasia, ecchymosis or bruising, cerebrovascular accident, confusion, equilibrium disorders, insomnia, muscle cramps, paresthesia, psychotic symptoms, shakiness, somnolence, arthralgia and rash, exanthema, hair loss, hyperkeratosis, macules, sweating, urticaria, Stevens-Johnson syndrome, erythema multiforme, blurred vision, gynecomastia, galactorrhea/hyperprolactinemia, increased urination, spotty menstruation, impotence.

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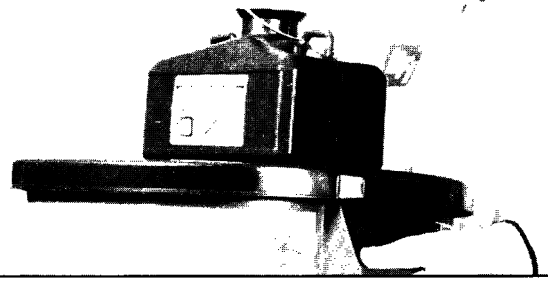

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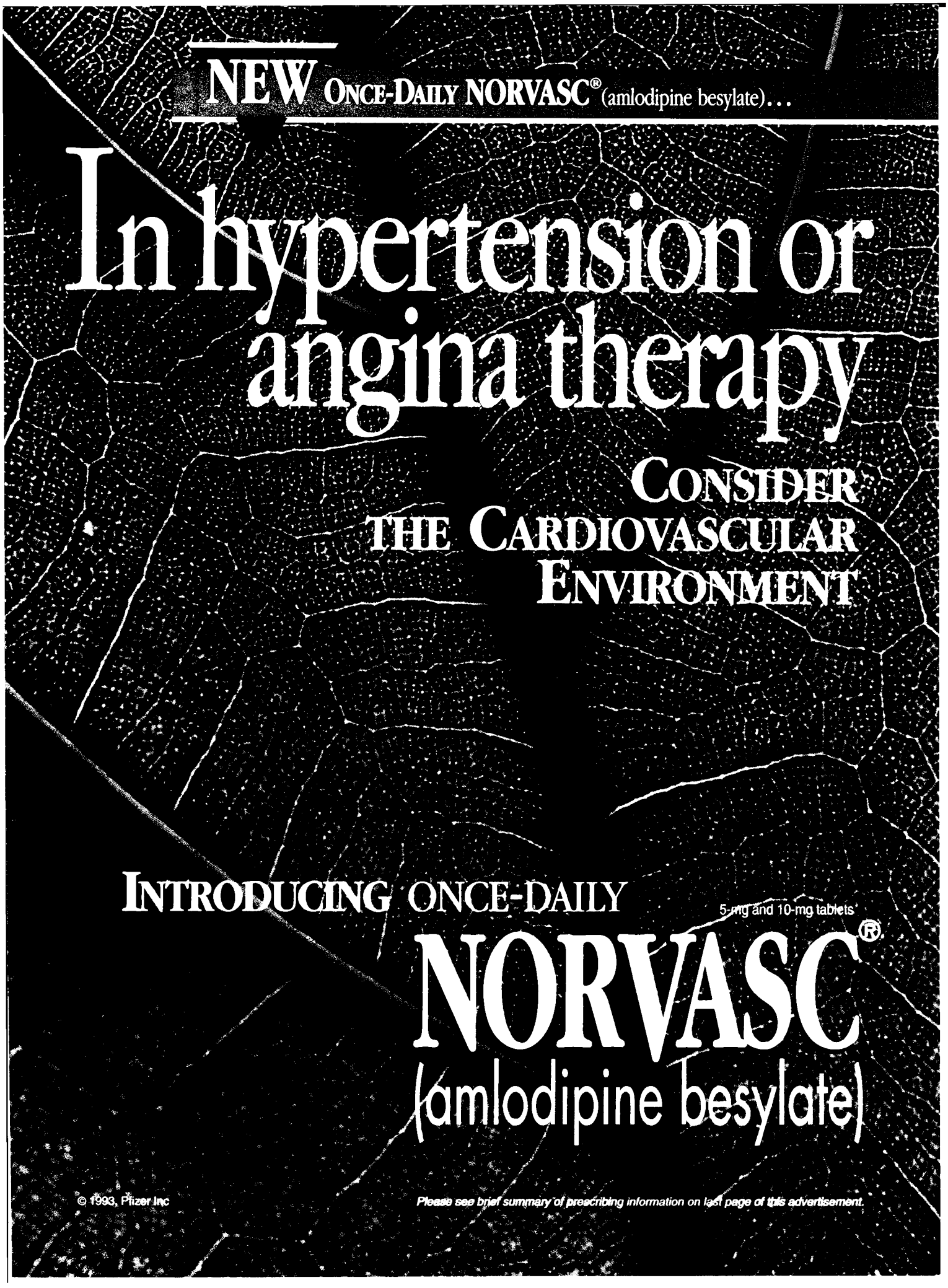
NEW ONCE-DAILY NORVASC® (amlodipine besylate)...
In hypertension or angina therapy
CONSIDER THE CARDIOVASCULAR ENVIRONMENT
INTRODUCING ONCE-DAILY
5-mg and 10-mg tablets
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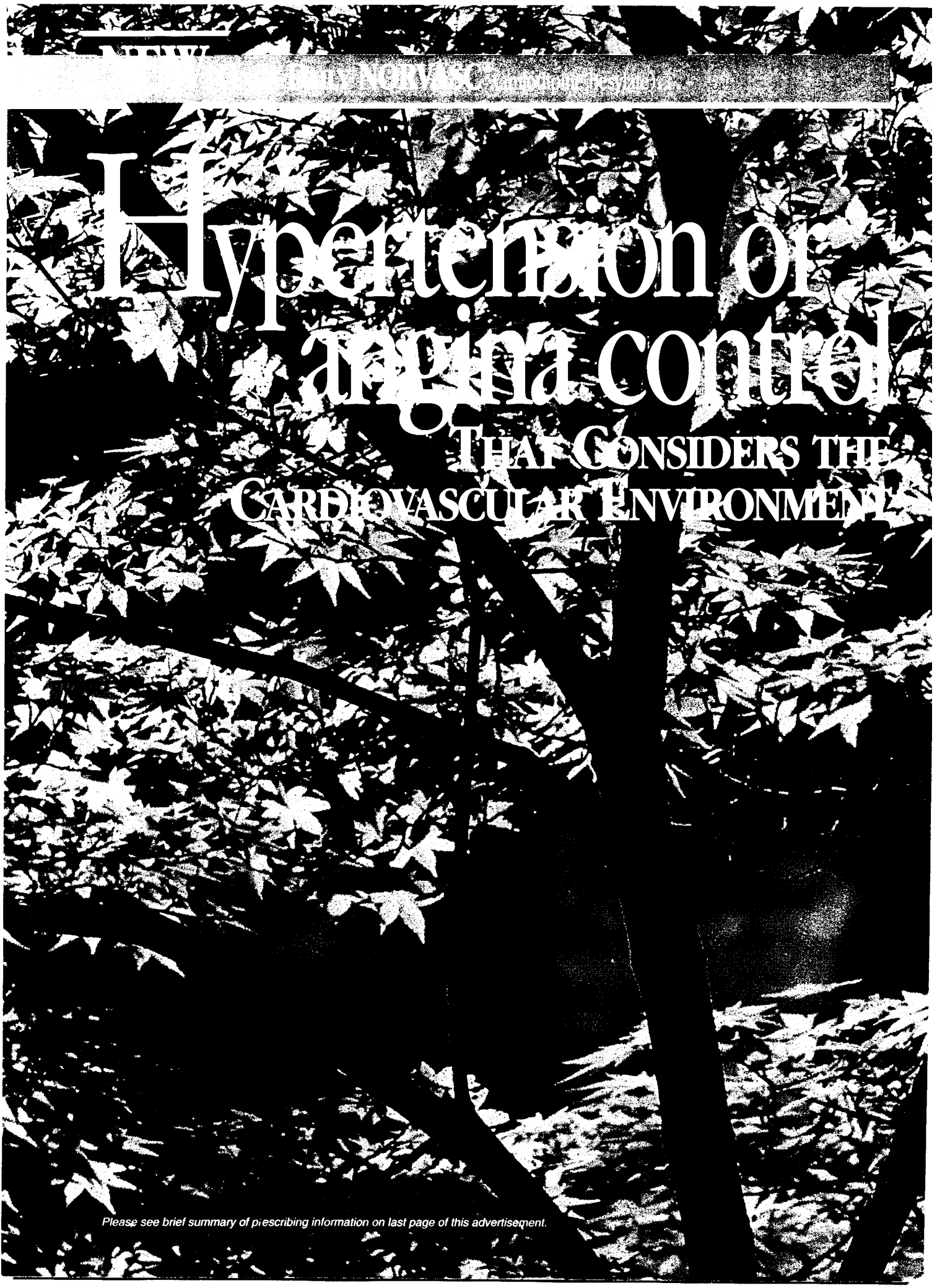
Hypertension or
angina control
THAT CONSIDERS THE
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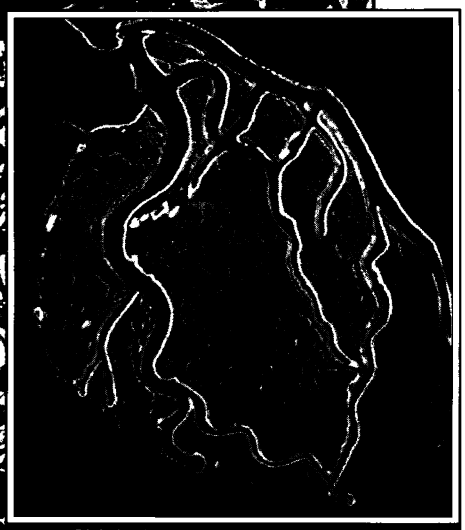
Please see brief summary of prescribing information on last page of this advertisement.



Digital subtraction angiography of the heart

NORVASC, a calcium channel blocker (CCB), provides effective yet gentle 24-hour control with intrinsic once-daily dosing[1]

Effective for mild, moderate, and severe hypertension[1]

- Over 80% of patients responding to NORVASC are controlled on 5 mg[1]
- 92% of patients remained on NORVASC for 1 year in a long-term study[2]

Effective for chronic stable and vasospastic angina[1]

- 24-hour angina protection, including the morning hours[1]
- Effective alone or in combination with beta blockers

Gradual onset of action and minimal adverse effects

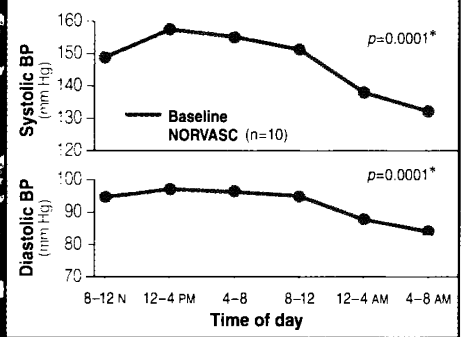
- No clinically significant effects on heart rate[1] or cardiac conduction[1]; no negative inotropic effects at clinical doses in hemodynamic studies,[‡] even when administered with beta blockers to humans[1]
- Has been used safely in patients with concomitant diseases
  - —Chronic obstructive pulmonary disease, well-compensated Class II-III congestive heart failure (CHF),[2] peripheral vascular disease, diabetes mellitus, and abnormal lipid profiles[1]
- Neutral effect on lipids[1]; no impairment of normal renal function[1]
- No drug interaction with digoxin, warfarin, or cimetidine[1]

Well tolerated: only 1.5% of patients in placebo-controlled trials (n=1730) discontinued NORVASC due to adverse effects[1]

- The most common side effects are headache and edema

[‡]Similar hemodynamic findings, however, have been observed with agents possessing significant negative inotropic effects.
[§]Therapy should be initiated with caution. See PRECAUTIONS section of brief summary.

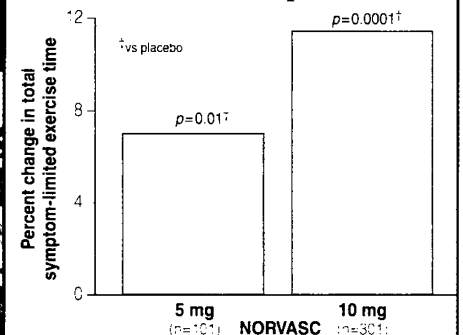
Mean blood pressure (BP) over 24 hours (week 4 data)[1]



Results of a double-blind, randomized, parallel, placebo-controlled study of NORVASC on ambulatory BP in 15 evaluable hypertensive patients (supine BP range 95 to 114 mm Hg). 10 on NORVASC, 5 on placebo. A 4-week single-blind placebo run-in period was followed by 4 weeks of double-blind therapy. Ambulatory BP was measured for 24 hours at the end of the placebo run-in phase and after double-blind therapy. Data on file.

*Average of mean BP values over 24 hours at week 4 versus baseline averages.

Change in symptom-limited exercise time measured 24 hours postdose[1]



Data from eight placebo-controlled, double-blind, randomized studies of the effect of NORVASC on symptom-limited exercise time. All studies included a 2-week single-blind placebo run-in period. The eight studies included five monotherapy trials and three add-on therapy trials. Treatment ranged from 4 to 8 weeks. Placebo group (n=297) had a 2.1% increase in symptom-limited exercise time. Exercise time at baseline: placebo 480 sec, 5 mg 523 sec, 10 mg 493 sec. Data on file.

NEW, ONCE-DAILY

5-mg and 10-mg tablets

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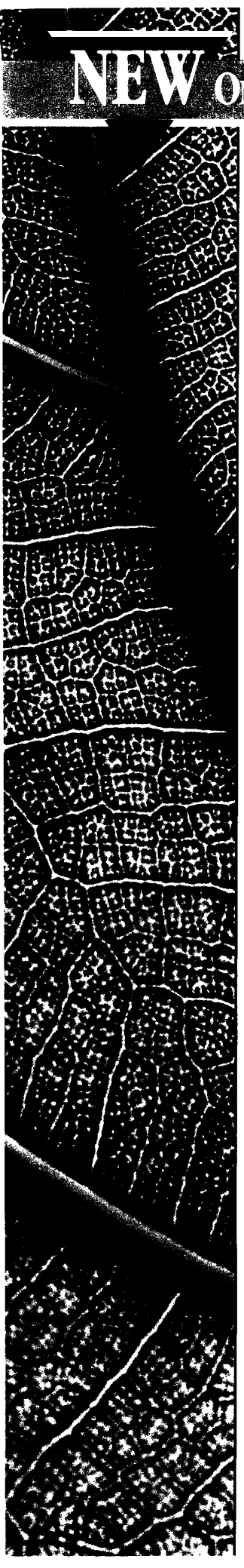
(amlodipine besylate)

CONFIDENT 24-HOUR CONTROL THAT CONSIDERS THE CARDIOVASCULAR ENVIRONMENT



HYPERTENSION OR ANGINA CONTROL THAT CONSIDERS THE CARDIOVASCULAR ENVIRONMENT

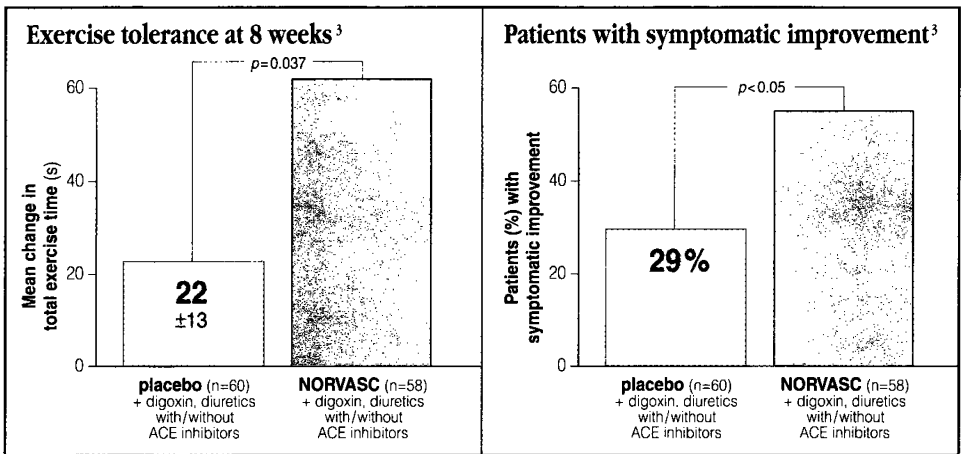
Well tolerated: only 1.5% of patients in placebo-controlled trials (n=1730) discontinued NORVASC due to adverse effects[1]

Dose-related side effects

Adverse event	NORVASC (%) 5 mg (n=296)	NORVASC (%) 10 mg (n=268)	placebo (%) (n=520)
Edema	3.0	10.8	0.6
Dizziness	3.4	3.4	1.5
Flushing	1.4	2.6	0.0
Palpitation	1.4	4.5	0.6

Caution should be exercised when using CCBs in any patient with heart failure

— In a double-blind study of 118 patients with mild to moderate CHF, NORVASC did not adversely affect cardiac function in patients with impaired LV function (LV ejection fraction < 40%)[3]



Results of a randomized, multicenter, double-blind, placebo-controlled trial of NORVASC in 118 patients with well-compensated CHF. All had New York Heart Association (NYHA) Class II or III symptoms, with LV ejection fractions < 40% (averaging 25%). NORVASC dose: 10 mg qd. Patients were already on therapy with digoxin and diuretics, and 80 patients were also taking angiotensin-converting enzyme (ACE) inhibitors. (Adapted from Packer M et al. *J Am Coll Cardiol*. 1991.) CHF patients did not have active angina or hypertension at the time of the study. Baseline exercise values: NORVASC, 570 sec; placebo, 613 sec. Symptomatology rating based on investigators' subjective global assessment. (Data on file.)

— In this study, NORVASC did not increase plasma norepinephrine levels, and ejection fraction did not change[3]

— Studies in patients with NYHA Class IV heart failure have not been performed

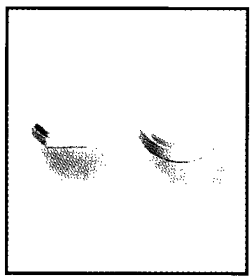
— NORVASC therapy, despite these findings, should be used with caution in patients with heart failure until safety in these patients can be confirmed with additional clinical experience

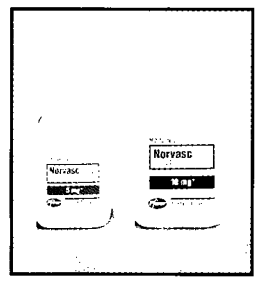
Please see brief summary of prescribing information on last page of this advertisement.

DOSING

Intrinsic once-daily dosing

- The usual starting dose is 5 mg in angina or hypertension
  - —In hypertension, small, fragile, or elderly individuals or patients with hepatic insufficiency may be started on 2.5 mg once daily
- Titration can proceed to 10 mg
  - —Most angina patients will require 10 mg
- Can be taken with or without food





Rx
Norvasc
5 mg #30
Sig: 1 tablet
daily

NEW, ONCE-DAILY

5-mg and 10-mg tablets

NORVASC®

(amlodipine besylate)

CONFIDENT 24-HOUR CONTROL THAT CONSIDERS THE CARDIOVASCULAR ENVIRONMENT

References:
1. Data on file. Pfizer Inc, New York, NY. **2.** The Treatment of Mild Hypertension Research Group. The treatment of mild hypertension study: a randomized, placebo-controlled trial of a nutritional-hygienic regimen along with various drug monotherapies. *Arch Intern Med.* 1991;151:1413-1423. **3.** Packer M, Nicod P, Khandheria BR, et al. Randomized, multicenter, double-blind, placebo-controlled evaluation of amlodipine in patients with mild-to-moderate heart failure. *J Am Coll Cardiol.* 1991;17:274A. Abstract.

Brief Summary
NORVASC® (amlodipine besylate) Tablets
For Oral Use

CONTRAINDICATIONS: NORVASC is contraindicated in patients with known sensitivity to amlodipine.

WARNINGS: Increased Angina and/or Myocardial Infarction: Rarely, patients, particularly those with severe obstructive coronary artery disease, have developed documented increased frequency, duration and/or severity of angina or acute myocardial infarction on starting calcium channel blocker therapy or at the time of dosage increase. The mechanism of this effect has not been elucidated.

PRECAUTIONS: General: Since the vasodilation induced by NORVASC is gradual in onset, acute hypotension has rarely been reported after oral administration of NORVASC. Nonetheless, caution should be exercised when administering NORVASC as with any other peripheral vasodilator particularly in patients with severe aortic stenosis.

Use in Patients with Congestive Heart Failure: Although hemodynamic studies and a controlled trial in NYHA Class II-III heart failure patients have shown that NORVASC did not lead to clinical deterioration as measured by exercise tolerance, left ventricular ejection fraction, and clinical symptomatology, studies have not been performed in patients with NYHA Class IV heart failure. In general, all calcium channel blockers should be used with caution in patients with heart failure.

Beta-Blocker Withdrawal: NORVASC is not a beta-blocker and therefore gives no protection against the dangers of abrupt beta-blocker withdrawal; any such withdrawal should be by gradual reduction of the dose of the beta-blocker.

Patients with Hepatic Failure: Since NORVASC is extensively metabolized by the liver and the plasma elimination half-life (t ½) is 56 hours in patients with impaired hepatic function, caution should be exercised when administering NORVASC to patients with severe hepatic impairment.

Drug Interactions: *In vitro* data in human plasma indicate that NORVASC has no effect on the protein binding of drugs tested (digoxin, phenytoin, warfarin, and indomethacin). Special studies have indicated that the co-administration of NORVASC with digoxin did not change serum digoxin levels or digoxin renal clearance in normal volunteers; that co-administration with cimetidine did not alter the pharmacokinetics of amlodipine; and that co-administration with warfarin did not change the warfarin prothrombin response time.

In clinical trials, NORVASC has been safely administered with thiazide diuretics, beta-blockers, angiotensin converting enzyme inhibitors, long-acting nitrates, sublingual nitroglycerin, digoxin, warfarin, non-steroidal anti-inflammatory drugs, antibiotics, and oral hypoglycemic drugs.

Drug/Laboratory Test Interactions: None known.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Rats and mice treated with amlodipine in the diet for two years, at concentrations calculated to provide daily dosage levels of 0.5, 1.25, and 2.5 mg/kg/day showed no evidence of carcinogenicity. The highest dose (for mice, similar to, and for rats twice* the maximum recommended clinical dose of 10 mg on a mg/m^2 basis), was close to the maximum tolerated dose for mice but not for rats.

Mutagenicity studies revealed no drug related effects at either the gene or chromosome levels.

There was no effect on the fertility of rats treated with amlodipine (males for 64 days and females 14 days prior to mating) at doses up to 10 mg/kg/day (8 times* the maximum recommended human dose of 10 mg on a mg/m^2 basis).

Pregnancy Category C: No evidence of teratogenicity or other embryo/fetal toxicity was found when pregnant rats or rabbits were treated orally with up to 10 mg/kg amlodipine (respectively 8 times* and 23 times* the maximum recommended human dose of 10 mg on a mg/m^2 basis) during their respective periods of major organogenesis. However, litter size was significantly decreased (by about 50%) and the number of intrauterine deaths was significantly increased (about 5-fold) in rats administered 10 mg/kg amlodipine for 14 days before mating and throughout mating and gestation. Amlodipine has been shown to prolong both the gestation period and the duration of labor in rats at this dose. There are no adequate and well-controlled studies in pregnant women. Amlodipine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: It is not known whether amlodipine is excreted in human milk. In the absence of this information, it is recommended that nursing be discontinued while NORVASC is administered.

Pediatric Use: Safety and effectiveness of NORVASC in children have not been established.

ADVERSE REACTIONS: NORVASC has been evaluated for safety in more than 11,000 patients in U.S. and foreign clinical trials. In general, treatment with NORVASC was well-tolerated at doses up to 10 mg daily. Most adverse reactions reported during therapy with NORVASC were of mild or moderate severity. In controlled clinical trials directly comparing NORVASC (N=1730) in doses up to 10 mg to placebo (N=1250), discontinuation of NORVASC due to adverse reactions was required in only about 1.5% of patients and was not significantly different from placebo (about 1%). The most common side effects are headache and edema. The incidence (%) of side effects which occurred in a dose related manner are as follows: edema (1.8% at 2.5 mg, 3.0% at 5.0 mg, and 10.8% at 10.0 mg, compared with 0.6% placebo); dizziness (1.1% at 2.5 mg, 3.4% at 5.0 mg, and 3.4% at 10.0 mg, compared with 1.5% placebo); flushing (0.7% at 2.5 mg, 1.4% at 5.0 mg, and 2.6% at 10.0 mg, compared with 0.0% placebo); and palpitation (0.7% at 2.5 mg, 1.4% at 5.0 mg, and 4.5% at 10.0 mg, compared with 0.6% placebo).

Other adverse experiences which were not clearly dose related but which were reported with an incidence greater than 1.0% in placebo-controlled clinical trials include the following: headache (7.3%, compared with 7.8% placebo); fatigue (4.5%, compared with 2.8% placebo); nausea (2.9%, compared with 1.9% placebo); abdominal pain (1.6%, compared with 0.3% placebo); and somnolence (1.4%, compared with 0.6% placebo).

For several adverse experiences that appear to be drug and dose related, there was a greater incidence in women than men associated with amlodipine treatment as follows: edema (5.6% in men, 14.6% in women, compared with a placebo incidence in men of 1.4% and 5.1% in women); flushing (1.5% in men, 4.5% in women, compared with a placebo incidence of 0.3% in men and 0.9% in women); palpitations (1.4% in men, 3.3% in women, compared with a placebo incidence of 0.9% in men and 0.9% in women); and somnolence (1.3% in men, 1.6% in women, compared with a placebo incidence of 0.8% in men and 0.3% in women).

The following events occurred in ≤1% but >0.1% of patients in controlled clinical trials or under conditions of open trials or marketing experience where a causal relationship is uncertain; they are listed to alert the physician to a possible relationship: **cardiovascular:** arrhythmia, bradycardia, chest pain, hypotension, peripheral ischemia, syncope, tachycardia, postural dizziness, postural hypotension; **central and peripheral nervous system:** hypoesthesia, paresthesia, tremor, vertigo; **gastrointestinal:** anorexia, constipation, dyspepsia,** dysphagia, diarrhea, flatulence, vomiting; **general:** asthenia,** back pain, hot flushes, malaise, pain, rigors, weight gain; **musculo-skeletal system:** arthralgia, arthrosis, muscle cramps,** myalgia; **psychiatric:** sexual dysfunction (male** and female), insomnia, nervousness, depression, abnormal dreams, anxiety, depersonalization; **respiratory system:** dyspnea,** epistaxis; **skin and appendages:** pruritus,** rash,** rash erythematous, rash maculopapular; **special senses:** abnormal vision, conjunctivitis, diplopia, eye pain, tinnitus; **urinary system:** micturition frequency, micturition disorder, nocturia; **autonomic nervous system:** dry mouth, sweating increased; **metabolic and nutritional:** thirst; **hemopoietic:** purpura.

The following events occurred in ≤0.1% of patients: cardiac failure, pulse irregularity, extrasystoles, skin discoloration, urticaria, skin dryness, alopecia, dermatitis, muscle weakness, twitching, ataxia. hypertonia, migraine, cold and clammy skin, apathy, agitation, amnesia, gastritis, increased appetite, loose stools, coughing, rhinitis, dysuria, polyuria, parosmia, taste perversion, abnormal visual accommodation, and xerophthalmia.

Other reactions occurred sporadically in single patients and cannot be distinguished from concurrent disease states or medications.

NORVASC therapy has not been associated with clinically significant changes in routine laboratory tests. No clinically relevant changes were noted in serum potassium, serum glucose, total triglycerides, total cholesterol, HDL cholesterol, uric acid, blood urea nitrogen, creatinine or liver function tests.

NORVASC has been used safely in patients with chronic obstructive pulmonary disease, well compensated congestive heart failure, peripheral vascular disease, diabetes mellitus, and abnormal lipid profiles.

OVERDOSAGE: Single oral doses of 40 mg/kg and 100 mg/kg in mice and rats, respectively, caused deaths. A single oral dose of 4 mg/kg or higher in dogs caused a marked peripheral vasodilation and hypotension.

Overdosage might be expected to cause excessive peripheral vasodilation with marked hypotension and possibly a reflex tachycardia. In humans, experience with intentional overdosage of NORVASC is limited. Reports of intentional overdosage include a patient who ingested 250 mg and was asymptomatic and was not hospitalized; another (120 mg) was hospitalized, underwent gastric lavage and remained normotensive; the third (105 mg) was hospitalized and had hypotension (90/50 mmHg) which normalized following plasma expansion. A patient who took 70 mg amlodipine and an unknown quantity of benzodiazepine in a suicide attempt, developed shock which was refractory to treatment and died the following day with abnormally high benzodiazepine plasma concentration. A case of accidental drug overdose has been documented in a 19 month old male who ingested 30 mg amlodipine (about 2 mg/kg). During the emergency room presentation, vital signs were stable with no evidence of hypotension, but a heart rate of 180 bpm. Ipecac was administered 3.5 hours after ingestion and on subsequent observation (overnight) no sequelae were noted.

If massive overdose should occur, active cardiac and respiratory monitoring should be instituted. Frequent blood pressure measurements are essential. Should hypotension occur, cardiovascular support including elevation of the extremities and the judicious administration of fluids should be initiated. If hypotension remains unresponsive to these conservative measures, administration of vasopressors (such as phenylephrine), should be considered with attention to circulating volume and urine output. Intravenous calcium gluconate may help to reverse the effects of calcium entry blockade. As NORVASC is highly protein bound, hemodialysis is not likely to be of benefit.

* Based on patient weight of 50 kg.
**These events occurred in less than 1% in placebo controlled trials, but the incidence of these side effects was between 1% and 2% in all multiple dose studies.

More detailed professional information available on request.
Revised August 1992

Pfizer

Pfizer Labs

Dr. Craig Watson
Medical Director, Comprehensive Epilepsy Services
Sutter General Hospital

YOU CAN'T WATCH YOUR EPILEPSY PATIENTS ROUND-THE-CLOCK. BUT WE CAN.

Even if you've made a positive diagnosis of epilepsy in patients who are suffering from seizures, the most effective treatment is sometimes elusive.

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Sutter Neuroscience Center at Sutter General Hospital offers a comprehensive in-patient program for epilepsy that permits precise diagnosis and treatment.

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The four-bed unit, which is the largest and most complete in the region, is designed for the comfort of the patients, who may need to be hospitalized for up to a week. Rooms are outfitted with a television, VCR and personal exercise equipment.

The program is designed for patients aged fifteen and older who have tried several different anti-convulsant medications, yet continue to experience seizures that interfere with their quality of life.

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For more about services or patient transfers, call Sutter Neuroscience Center at Sutter General Hospital in Sacramento, (916) 455-4323.

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Clinical response rate of 98% in bronchitis and pneumonia[1]

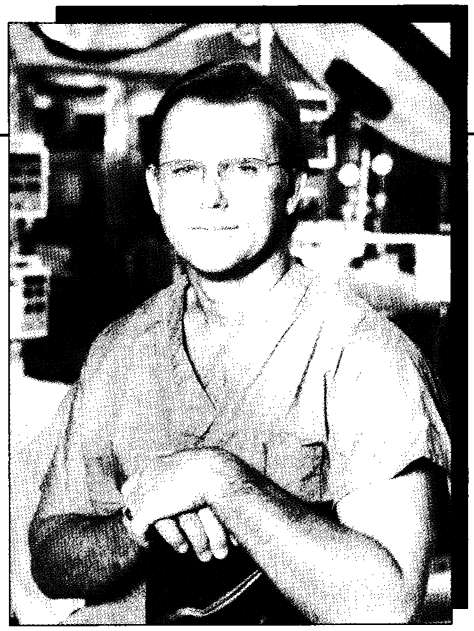
† For susceptible strains of indicated organisms.
* *In vitro* activity does not necessarily imply *in vivo* efficacy.

Please see brief summary of prescribing information for contraindications, warnings, precautions and adverse reactions on the previous page.

References: 1. Data on file, SmithKline Beecham Pharmaceuticals. **2.** Brown R, Pinkerton R, Tuttle M. Respiratory infections in smokers. *Am Fam Physician* 1987;36:133-140. **3.** Neu HC. Contribution of beta-lactamases to bacterial resistance and mechanisms to inhibit beta-lactamases. *Am J Med* 1985;79 (suppl 5B):2-12.

SB SmithKline Beecham Pharmaceuticals
Philadelphia, PA 19101

PACE PROFILE



Vaughn A. Starnes, M.D. has joined the University of Southern California School of Medicine.

Vaughn A. Starnes, M.D., has joined the University of Southern California School of Medicine as Professor of Surgery, Chief of the Division of Cardiothoracic Surgery and Director of the USC Cardiothoracic Center at USC University Hospital, Childrens Hospital Los Angeles and Los Angeles County+USC Medical Center. Dr. Starnes is a world-recognized leader and innovator in adult and pediatric heart, heart-lung and lung transplantation and treatment of congenital heart disease.

In 1984 Dr. Starnes was accepted to the Stanford Cardiothoracic program, where he completed two years as a resident in cardiovascular surgery, and one year as chief resident in cardiac transplantation under the guidance of Norman Shumway, M.D.

In 1988 Dr. Starnes was appointed director of Stanford's heart-lung transplantation program, and later became chief of pediatric heart surgery and director of the transplant program at Stanford's Lucile Salter Packard Childrens Hospital. He performed about 400 adult and pediatric cardiac cases annually at Stanford. In addition to his adult cardiothoracic surgical expertise, Dr. Starnes earned a national reputation for his work in pediatrics.

Dr. Starnes also pioneered lung and heart-lung transplant procedures in children that previously had only been performed on adults. In 1991 he was the first surgeon to transplant the left upper lobe of a 2-year-old donor into a newborn with pulmonary hypertension who could not be weaned off ECMO (Extracorporeal Membrane Oxygenation). In 1992, he performed the first lung transplant on a baby with congenital diaphragmatic hernia.

University of Southern California

USC Cardiothoracic Center

New Era of Excellence

The arrival of Vaughn A. Starnes, M.D., at the University of Southern California School of Medicine marks a new era of excellence in the treatment of cardiovascular disease. This commitment is exemplified in the creation of the USC Cardiothoracic Center at USC University Hospital, Childrens Hospital Los Angeles and Los Angeles County+USC Medical Center.

Comprehensive Services

The USC Cardiothoracic Center is one of a handful of centers in the country to provide a comprehensive range of adult and pediatric cardiovascular services including adult and pediatric heart, heart-lung and lung transplantation.

The Center features a non-invasive vascular diagnostic laboratory, diagnostic angiography laboratory and state-of-the-art cardiac catheterization laboratories. If indicated, cardiac surgeons incorporate the latest corrective surgical techniques for conditions such as ventricular and atrial arrhythmias and aortic diseases that involve aneurysms and dissections.

The Center also specializes in the treatment of infants with congenital heart defects including hypoplastic left heart syndrome, aortic valve disease, and transposition of the great vessels.

Collaboration of Specialists

At the Center, cardiologists, cardiothoracic surgeons, vascular surgeons, anesthesiologists, radiologists, interventional radiologists and allied medical professionals pool their extensive knowledge and expertise to provide patients with the full range of diagnostic and treatment alternatives.

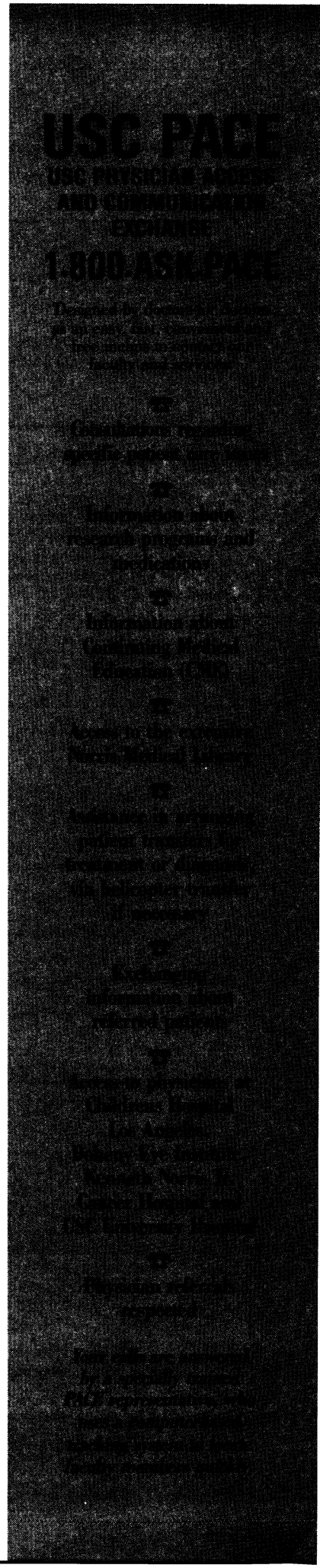
Goal-Directed Research

As a university-based program, the Center is actively engaged in research. Specialists identify clinical problems and then seek the answer in the laboratory. Patients benefit from this link between bench and bedside, which promises to provide a better understanding of the physiology of the disease process.

Community Resource

As a vital component of the USC School of Medicine, the USC Cardiothoracic Center serves as a key educational resource for community-based and referring physicians. Physicians are encouraged to contact the Center through PACE to obtain telephone consultations, and access information regarding new patient care techniques, medications and research protocols to receive assistance with patient management concerns.

A new era is unfolding at the USC School of Medicine. We invite you to be a part of it. For more information about the USC Cardiothoracic Center, or to refer a patient, dial:
1-800-ASK-PACE (275-7223).



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PEDIATRICS. Community health center serving a predominantly Hispanic, underserved inner city population seeking to expand its Primary Care physician staff. Tremendous job satisfaction; San Diego lifestyle; loan repayment possible. Contact Joseph Browne, MD, Medical Director; Logan Heights Family Health Center, 1809 National Ave, San Diego, CA 92113.

BC/BE GENERAL INTERNIST NEEDED. Nine physician department in 27 doctor multispecialty clinic. Guaranteed salary. Excellent benefits. CV to Mike McCraley, Ogden Clinic, 4650 Harrison, Ogden, UT 84403; (800) 234-5637.

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PHYSICIANS NEEDED

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MONTEREY BAY. Midway between Santa Cruz and Monterey, this unpretentious community is perfect for the hiker, biker, surfer, and outdoorsperson. Medical staff is anxious to welcome additional BE/BC physicians in Family Practice, Pulmonary Medicine, Pediatrics, and Infectious Disease. Group and independent practice with call schedule which allows time for lifestyle. Contact Ken Baker, Physician Search Group, 550 Montgomery St, Ste 725, San Francisco, CA 94111; (800) 229-0411 or FAX (415) 399-0411.

WARM AND SUNNY ARIZONA. Thomas-Davis Medical Centers, an expanding multispecialty group of 190 plus physicians, needs BC/BE Pediatrics, Internal Medicine, Family Practice, OB/GYN, Urgent Care, General Surgery, Orthopedic Surgery, Urology, and Ophthalmology physicians. Top benefits, profit sharing, guarantee first two years, plus incentive pay, early shareholder. Fee-for-service plus HMO. BE/BC. Call or write Bill De Long; (800) 658-9166, TDMC, PO Box 12650, Tucson, AZ 85732.

CALIFORNIA, PACIFIC NORTHWEST, ARIZONA. Positions in Family Practice, Internal Medicine, Orthopedics, Pediatrics and OB /GYN. Call or send confidential CV to Mitchell & Associates, Inc, PO Box 1804, Scottsdale, AZ 85252; (602) 990-8080.

(Continued on Page 211)

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CALIFORNIA

Primary Care Physicians and Radiologists needed to work as locum tenens statewide. High salary, paid malpractice. Work whenever and wherever you wish. Permanente placements as well. **INTERIM PHYSICIANS, formerly Western Physicians Registry; Northern California, contact Jim Ellis, (800) 437-7676. Southern California, contact Tracy Zweig, (800) 635-3175.**

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THE VA MEDICAL CENTER, PRESCOTT, ARIZONA is seeking a BC/BE Internist with or without subspecialty. Regular hours. Experience with Holter monitors, treadmill testing, and/or endoscopy desirable but not necessary. Prescott is a lovely area with beautiful surroundings, clean air, pleasant lifestyle, wonderful dry four season climate. Interested physicians may call (602) 445-4860, ext 6640, or send CV to Robert Parsons, MD, Acting Chief, Medical Service, VA Medical Center, Prescott, AZ 86313. An equal opportunity employer.

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(Continued on Page 212)

(Continued from Page 211)

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FAX: (509) 482-2187

SALT LAKE CITY–URGENT CARE/FAMILY PRACTICE. Six year old center in upper middle class community. BC preferred, early partnership available. Great recreation area. Work Net, PO Box 26692, Salt Lake City, UT 84199.

BC/BE FAMILY PRACTITIONER with interest in OB and a commitment to caring for the underserved, needed to join clinics in Milton-Freewater, and Hermiston, Oregon. Diverse cultural influences. Rural setting, abundant recreational opportunities. Competitive salary, Public Health Service loan repayment slots, professional liability, excellent benefit package including vacation up to 32 days per year. Contact Ann Garza, Director of Personnel, or Jeri Weeks, Recruiting Specialist, at (509) 865-5898, or Sylvia Arroyo, Clinic Administrator, (509) 525-6650.

ARIZONA. Hospital sponsored solo opportunities for Family Practitioners and Internists. Excellent compensation with ample coverage. Well-equipped facility including MRI and CT. Send CV or contact Mitch Young, PO Box 1804, Scottsdale, AZ 85252; (602) 990-8080; FAX (602) 990-8513.

INTERNAL MEDICINE. Community health center serving a predominantly Hispanic, underserved inner city population seeking to expand its Primary Care physician staff. Tremendous job satisfaction; San Diego lifestyle; loan repayment possible. Contact Joseph Browne, MD, Medical Director; Logan Heights Family Health Center, 1809 National Ave, San Diego, CA 92113.

(Continued on Page 213)

Chief of Disease Control

Salary $76,086 to $94,265 annually

Plus $275.00/month Health Benefit Package

Riverside County Health Services Agency, Department of Public Health is recruiting for a Chief of Disease Control to be responsible for the Disease Control Branch of the Public Health Department. To qualify candidates must possess a valid Physician's and Surgeon's Certificate issued by the State of California. And, Option I: Certification or eligibility for certification in one of the medical specialties recognized by the American Specialty Board, OR, Option II: Three years of experience as a physician in a public health care agency. (Possession of a Master's Degree in Public Health or a closely related field may be substituted for 1 year of the required experience.) Two or more years of experience working in infectious disease control in a public health setting is highly desirable. Resumes and/or County applications materials must be received no later than 5:00 p.m. Friday, March 5, 1993. For more information and application materials, contact:

Riverside County Personnel Department
Room 109
P.O. BOX 1569
Riverside, CA 92502-1569
EEO AA M/F/D/V

SAINT JOSEPH

New Mexico

Excellent opportunity for board certified or board eligible OB/GYN, Pediatric, Internal Medicine and Family Practice physicians to practice within MED-NET (Medical Network of New Mexico), an integrated health care system. Enjoy sunshine, skiing, hiking, fishing and hunting in a Southwestern lifestyle. For further information contact Anne Winter, Director of Professional Development, The St. Joseph Healthcare System, Albuquerque, New Mexico.

(505) 246-8003

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PHYSICIANS WANTED

FAMILY PHYSICIAN–LEWISTON, IDAHO Opportunity to join Family Practice group. Ambulatory and acute/inpatient care. No OB. Competitive income guarantee with opportunity to join full partnership. Send CV to Clearwater Medical Clinic, 1522 17th St, Lewiston, ID 83501, attn: Peggy Johnson; or call (208) 743-8416.

ROCKY MOUNTAIN WEST AND SOUTHWEST NEED PHYSICIANS. All specialties needed. Urban, rural, solo, group opportunities, all close to mountain recreation. Call Rita Longino at (800) 279-5267 or FAX CV to (800) 467-1246 or send CV to WHS, PO Box 2107, Corrales, NM 87048-2107.

NORTHERN CALIFORNIA RECREATION AREA. Multispecialty group has immediate opening for an Internal Medicine practitioner with a particular interest in Critical Care. Clinical activities involve full range of Internal Medicine outpatient and inpatient practice. Beautiful northern California location offers abundant recreational opportunities as well as small town living. Competitive salary and comprehensive benefit package. Please send CV to 10978 Donner Pass Rd, Truckee, CA 96161.

CALIFORNIA–CHICO. MEDICAL DIRECTOR for busy Emergency Department with annual volume of 16,000 and growing. Successful Occupational Medicine program. The successful applicant shall be BC in Internal Medicine or Emergency Medicine, ACLS/ATLS. Guaranteed compensation with incentives. Malpractice paid. Send r sum in confidence to Administrator, Chico Community Hospital, 560 Cohasset Rd, Chico, CA 95926. FAX (916) 894-6428.

PHYSICIANS WANTED

ORTHOPEDIC SURGEON

Valley Medical Center of Fresno, a Primary teaching hospital for the University of California, San Francisco—Fresno Medical Education Program, seeks a BC/BE Orthopedic Surgeon to fill a faculty/staff position. Eligibility for a UCSF academic clinical appointment preferred. The Orthopedic Department at VMC supports a busy level one trauma center and actively participates in teaching residents in General Surgery, Emergency Medicine, and Family Practice. Competitive salary and benefits. Central California location offers enjoyable and affordable year-round recreational living with easy mountain and coastal access.

Address inquiries to **Richard A. Lockwood, MD, Assistant Dean/Director of Medical Affairs, 445 S Cedar, Fresno, CA 93702.** Equal opportunity employer; women and minorities are encouraged to apply.

OTOLARYNGOLOGIST. BC/BE to join 28 physician multispecialty group practice. Located in beautiful Pacific northwest between Seattle and Vancouver, BC. Contact Shane Spray, 1400 E Kincaid, Mount Vernon, WA 98273.

FAMILY PRACTICE. Seeking Family Practice or General Practice physician for rapidly growing area in northern Arizona — Bullhead City, Arizona/Lauglin, Nevada. Opportunity unlimited. Compensation unlimited. Malpractice and health insurance. Send CV to Bullhead Medical Center, 1648 Highway 95, Bullhead City, AZ 86442, or FAX to (602) 763-1311.

PHYSICIANS WANTED

MOUNTAIN VIEW. BC/BE Family Physician to join thriving four member Family Practice group located in the heart of the Silicon Valley. Practice includes Surgery and Obstetrics. C-sections are OK. Excellent salary and benefits. Contact Dianne Higgins, MD, 253 Franklin St, Mt View, CA 94041; (415) 967-5591.

OB/GYN. Multispecialty group in northwest Washington desires second Obstetrician. Excellent practice opportunity, full range of benefits, early partnership status, all practice costs paid. For more information contact Shane Spray, 1400 E Kincaid, Mount Vernon, WA 98273; (206) 428-2524.

MONTEREY, CALIFORNIA. BC/BE Internist needed to replace retiring partner in busy four member group. Reply to Number 273, Western Journal of Medicine, PO Box 7602, San Francisco, CA 94120-7602.

FAMILY PRACTICE PHYSICIAN. Full-time in a busy walk-in medical clinic. Located in Visalia, California (Tulare County). Malpractice insurance, good salary, etc. Please call (209) 627-5555 for more information.

ASSOCIATE IN PEDIATRICS. Kern Medical Center, Bakersfield, California, a teaching hospital affiliated with UCLA and UCI Schools of Medicine, seeks an Associate in the Division of Pediatrics. Prerequisites include eligibility or certification by the American Board of Pediatrics, strong interest in teaching and qualifications for faculty appointment in UCLA Department of Pediatrics. Comprehensive salary and benefit package. A part-time private practice is permitted. Medical center is in central California, a mid-sized urban community with moderate cost of living. Send CV and inquiries to Navin Amin, MD, Chairman, Department of Family Practice/Pediatrics, Kern Medical Center, 1830 Flower St, Bakersfield, CA 93305.

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PHYSICIANS WANTED

PHYSICIANS WANTED

PHYSICIANS WANTED

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PHYSICIANS WANTED

KAISER PERMANENTE

Good People. Good Medicine.

NORTHERN CALIFORNIA

Several positions available for Internal Medicine, most medical subspecialties, ENT, Orthopedics, Anesthesiology, and OB/GYN. We are a young, aggressive group in a well known prepaid group practice HMO organization with excellent benefits and a very reasonable call schedule. You will have a rewarding practice opportunity with ample time to enjoy the mountains and San Francisco which are nearby. If interested please call or send CV to Physician Recruitment, Administration, The Permanente Medical Group, Inc, 1305 Tommydon St, Stockton, CA 95210; (209) 476-3300.

NORTHERN CALIFORNIA. Opportunities available with Comprehensive Medical Evaluations in Sacramento, San Jose, and Monterey bay area for BC physicians in Orthopedic Surgery, Psychiatry, Internal Medicine, and subspecialties, Dermatology, Neurology, Physical Medicine/Rehabilitation, Ophthalmology,Otolaryngology, Plastic/Reconstructive Surgery and Toxicology/ Occupational Medicine, to perform forensic medical evaluations. This is an excellent opportunity to supplement income without increasing your practice overhead. Send inquiry to Terence Doyle, Comprehensive Medical Evaluations, 87 Scripps Dr, Ste 308, Sacramento, CA 95825; or call (916) 567-3411.

CALIFORNIA–THE LAST FRONTIER may be located in the foothills of the Sierra Mountains in northern California within minutes of Modesto. If you are an Internist or Family Physician who practices quality medicine and enjoys independence, please contact Ken Baker, Physician Search Group, 550 Montgomery St, #725, San Francisco, CA 94111; (800) 229-0411, FAX (415) 399-0411.

FAMILY PRACTICE RESIDENCY FACULTY POSITION, FULL-TIME ASSISTANT PROFESSOR, UNIVERSITY OF WYOMING FAMILY PRACTICE RESIDENCY PROGRAM–CASPER. The University of Wyoming Family Practice Residency Program at Casper is a well established Family Practice residency program with 24 residents and nine faculty members known for developing outstanding rural physicians. Casper is centrally located in the state and is home to the Wyoming Medical Center, the affiliated hospital for the program, and the major medical referral center for the state. Casper offers the advantages of living in a small city that lacks the usual urban problems. Responsibilities include resident supervision in ambulatory and inpatient settings, participation in clinical research projects, direct patient care, and administrative duties. Requirements include BC, a minimum of three year's experience in Family Practice, including Obstetrics, and a strong desire to teach rural Family Medicine. Applicants should include current CV and three references. Competitive salary and benefits. Come join us in beautiful Wyoming. The University of Wyoming is an equal opportunity/affirmative action employer. Final approval will be made by the University of Wyoming. Please contact Joe Schoeber, MD, Acting Program Director, University of Wyoming, Family Practice Residency Program—Casper, 1522 E. A St, Casper, WY 82601; (307) 266-3076.

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PHYSICIANS WANTED

ORTHOPEDIC SURGEONS. Orthopedic Surgeon for a very busy Orthopedic service in a 223-bed teaching hospital with residencies in General Surgery, Internal Medicine, OB/GYN, and Family Practice. Should be BC/BE. Experience in arthroscopy preferred. Salary and compensation plan negotiable depending on experience. Hospital located in beautiful northern San Joaquin Valley close to major cities and skiing areas. Please submit CV and references or contact Nathaniel Matolo, MD, Chief of Surgery, San Joaquin General Hospital, PO Box 1020, Stockton, CA 95201; phone (209) 468-6600. AA/EOE.

NORTHERN CALIFORNIA HOSPITAL seeking a BC/BE Internist to staff its new satellite medical clinics. Assistance is available in establishing a practice. Net income guarantees are open including support for office staff and required equipment. Contact Margaret Ward, Redbud Community Hospital, PO Box 6720, Clearlake, CA 95422; (707) 994-6486, ext 128.

ESCAPE THOSE URBAN HASSLES and come to scenic northern California, southern California, and Phoenix, Arizona. Opportunity available to join two other Internists in private practice. Competitive salary and benefit package available. Contact Mark Oswald of Gielow Associates, 306 N Milwaukee St, Milwaukee, WI 53202; (800) 969-7715, FAX (414) 226-4131. Confidential inquiries welcome.

IDAHO. BC Family Practitioner to join Family Practice Group (OB required) in university town of 50,000. Good benefits and competitive first year salary, then association. Interest in resident and medical student teaching. Contact Michael S. Baker, MD, 755 Hospital Wy, Ste A4, Pocatello, ID 83201; telephone (208) 233-7000.

PHYSICIANS WANTED

PART-TIME MEDICAL CONSULTANT CONTRACTS

Physicians needed to work under contract, on a part-time basis for the Social Security Administration's Disability Insurance Program. Involves review of medical evidence in disability claims at 75 Hawthorne Street, San Francisco, California. No patient contact. Applicants must: (1) have a valid license to practice medicine in the USA; (2) have current or recent clinical experience; and (3) be available between 6:30 am and 5:30 pm Monday through Friday for case review. Subject to change, the specialties needed are Psychiatry and Psychology. Women and minorities are encouraged to apply. If interested in receiving further information, submit written request by March 5, 1993 to:

Contracting Officer
50 United Nations Plaza, Room 403
San Francisco, CA 94102

SAN FRANCISCO BAY AREA–PEDIATRICIAN. Recently trained, energetic, enthusiastic, BC preferred, for 18 physician Palo Alto Medical Clinic satellite. Clinic is progressive 150 physician multispecialty group known for innovation and excellence. Practice is established and growing. Excellent location, convenient access to San Francisco and Stanford. Excellent compensation/benefits package. Please send CV and letter of interest to David Hooper, MD, Medical Director, Palo Alto Medical Foundation, 39500 Liberty St, Fremont, CA 94538.

PHYSICIANS WANTED

INTERNAL MEDICINE

Pick your own Internal Medicine Practice—group, solo, partnership, hospital-based or not. Urban, suburbs, rural. Many opportunities for 93 residents. FAX CV to Medical Staffing Associates, (800) 4-FAXDOC, (800) 432-9362, or call (800) 3-MSADOC, (800) 367-2362.

TACOMA. GROUP PRACTICE opportunity available for an energetic Internist. Established six physician call schedule, offices on hospital campus, strong payor mix, very affordable lifestyle. Excellent remuneration package with future partnership. Contact Ken Baker, Physician Search Group, 550 Montgomery St, Ste 725, San Francisco, CA 94111; (800) 229-0411 or FAX (415) 399-0411.

OB/GYN. Community health center serving a predominantly Hispanic, underserved inner city population seeking to expand its Primary Care physician staff. Tremendous job satisfaction; San Diego lifestyle; loan repayment possible. Contact Joseph Browne, MD, Medical Director; Logan Heights Family Health Center, 1809 National Ave, San Diego, CA 92113.

WESTERN MONTANA. BC/BE General Internist with interest in Primary Care wanted for active 50 plus physician multispecialty group. Unparalleled outdoor recreation and outstanding schools in university town of 45,000. Income guarantee, malpractice insurance, early partnership. Excellent fringe benefits. Needed for summer/fall 1993. Send CV to Administrator, Western Montana Clinic, PO Box 7609, Missoula, MT 59807.

URGENT CARE/PRIMARY CARE PHYSICIANS. Current permanent positions available in Phoenix, Denver, Colorado Springs. Attractive settings with reasonable workload. Enticing locum tenens assignments available also throughout the Rocky Mountain west. Call or write Ed Novelli, Interim Physicians, 4155 E Jewell, Ste 1018, Denver, CO 80222; (800) 669-0718.

WASHINGTON. Openings for career oriented Emergency Physicians, BC in Emergency or Primary medical specialty. Seattle metropolitan hospital with 54,000 annual visits. Excellent salary in a stable growing group. Contact Maurice Montag in care of Tammie Johnson, 8009 S 180th, Ste 110, Kent, WA 98032; (206) 575-2595.

SEATTLE. BC/BE GENERAL INTERNIST to join growing practice of BC Internists anticipating a full-time practice on Mercer Island. Financial income advances available; associate status with no buy-in for minimum one year; group and location excellent. Write Christine J. Robertson, MD, 3236 78th Ave SE, Ste 104, Mercer Island, WA 98040.

TWO INVASIVE CARDIOLOGISTS AND FAMILY PHYSICIANS NEEDED. Unique opportunity. Gorgeous California central coast. Partnership within year. Send references/CV to PO Box 220, 395 Del Monte Center, Monterey, CA 93940.

INTERNAL MEDICINE—Southern California. Challenging career opportunities for specialists in Internal Medicine desiring private practice. Growing, prestigious, university-affiliated south bay medical center is recruiting BC/BE physicians for expanding solo and group practices. Excellent compensation. Submit CV to J. Michaels, 2600 Cliff Dr, Newport Beach, CA 92663.

PEDIATRICIANS–Southern California. Challenging career opportunities for Pediatricians desiring private practice. Growing, prestigious, university-affiliated south bay medical center is recruiting BC/BE physicians for expanding solo and group practices. Excellent compensation. Submit CV to J. Michaels, 2600 Cliff Dr, Newport Beach, CA 92663.

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PHYSICIANS WANTED

PHYSICIAN OPPORTUNITIES IN CALIFORNIA AND NATIONWIDE

Call (800) 727-2478 or FAX your CV in complete confidence to (408) 727-7390. Never a fee to the physician. **Nugent & Grant, 1400 Coleman Ave, Ste B24, Santa Clara, CA 95050.**

INTERNAL MEDICINE/PRIMARY CARE. BC/BE, recently trained (university program preferred) for group practice in San Francisco. Send CV and availability to A. Aronow, MD, 45 Castro St, San Francisco, CA 94114.

OB/GYN—Southern California. Career opportunities for ambitious Obstetricians desiring private practice. Growing, prestigious, university-affiliated south bay medical center is recruiting BC/BE physicians for expanding solo and group practices. Excellent compensation. Submit CV to J. Michaels, 2600 Cliff Dr, Newport Beach, CA 92663.

POSITION WANTED

INDUSTRIAL MEDICINE. Experienced and highly recommended MD seeks full-time employment as in-house consultant to WC insurance carrier or in-plant/clinic. Milieu preferably in San Francisco bay area; will consider others. Superb results in conservative care of carpal tunnel syndrome, retention of case management, and significant cost containment. Certified in surgical specialty, no malpractice history, probity, and available now. Write 1880 California St, #8, San Francisco, CA 94109.

PLACEMENT SERVICES

NURSE PRACTITIONERS PHYSICIAN ASSISTANTS

Western Practitioner Resources is California's most active and respected service exclusively for the placement of mid-level practitioners. References are available from your colleagues.

Heidi Bourne, RN, Director
(707) 822-0990; (800) 345-5859

PRACTICES AVAILABLE

SAN DIEGO COUNTY. Family, Internal, OB/GYN, clinics, and Pediatric practices available. Long established—doctors retiring. Various prices and low down payments. Call CBI, San Diego County's professional practice sales specialists, (619) 283-7009.

SAN BERNARDINO, CALIFORNIA. FAMILY PRACTICE. Well established, 22-year-old Family Practice for sale in fast growing area. Close proximity to two major teaching hospitals and three private hospitals. Great family area with plenty of outdoor recreation. Doctor relocating but will assist with patient introductions. Many options open for this one-stop Family Clinic. Call (714) 644-1230, FAX (714) 884-0345.

LARGE FAMILY PRACTICE in Aurora, Colorado. Also would be excellent Internal Medicine Practice. $350,000 gross with potential for much more. Denver suburb with great outdoor activities. Marvin N. Cameron, MD; (303) 364-4553 or (303) 740-7680.

LOS ANGELES, CALIFORNIA. General Practice available. Fully equipped building with x-ray, Physical Therapy, EKG, and laboratory. Building for sale or lease. Practice included. Contact Gerald Klaz, MD, PO Box 1525, Gateway Station, Culver City, CA; (213) 650-5950.

PRACTICES AVAILABLE

PHYSICIAN IN GENERAL PRACTICE wishes to retire. Looking for doctor to take over practice, office staff, and rent his building. Call (209) 674-4717.

FAMILY–GENERAL PRACTICE. Three miles to open staff hospital, 28 miles north of Palm Springs, California. Gross 200k per year, without hospital. No OB. Building and equipment sale or lease. Reason for sale—retiring. James S. Burrell, MD, PO Box 728, Joshua Tree, CA 92252.

OFFICE SPACE

SAN FRANCISCO—Stonestown Medical-Dental Building. Established facility with good referrals. Adjacent to Stonestown Galleria at 19th Avenue. Excellent public transportation and free parking. Call (415) 564-8848.

MONTEREY–CASS STREET. Prime medical space—1208 square feet. High image building with on-site parking. Five medical specialties represented. Landlord will contribute to space renovation. Contact Michael Tancredi, Mahoney-Tancredi Co; (408) 646-1919.

VACATION RENTALS

PUERTO VALLARTA TWO BEDROOM, two bath penthouse, 1,900 square feet, full kitchen at the Krystal. $185 per night. All amenities. Call Janis, (714) 364-9148 evenings or weekends.

FIND THE RIGHT PHYSICIAN for your needs through WJM Classified Advertising; (415) 882-3376.

LOCUM TENENS

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The deadline for submitting classifieds for the **April** issue of WJM is **March 1.** Send your advertisement to:

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BOOKS

PATENTS

MEDICAL DEVICES and procedures a specialty. Consult a registered patent attorney before you publish or practice your invention. Acronational Patent Law Firm, One Market Plaza, Spear Street Tower, Ste 900, San Francisco, CA 94105; (415) 777-9017.

MEDICAL EQUIPMENT

ABODIA LIGHTED SLIDE STORE AND VIEW. Store 1,000 to 10,000 on lighted racks before a viewing panel. Organize your slides and use them! Catalog, call (800) 950-7775.

MEDICAL EQUIPMENT

CLOSED GYNECOLOGIC OFFICE. Must sell late model exam tables, stools, large and small desks, secretarial chairs, reception room furniture. Almost new. Call (408) 448-1446.

CONFERENCES

RETREAT FOR PHYSICIANS. March 26-28, 1993. Jesuit Retreat House. 300 Manresa Wy, Los Altos, CA 94022. Call (415) 948-4491.

FAMILY PRACTICE DAY
MARCH 12, 1993
8:30 AM - 5:00 PM
SWEDISH MEDICAL CENTER
GLASER AUDITORIUM
(206) 386-2265

AMERICAN COLLEGE OF CARDIOLOGY announces the 42nd Annual Scientific Session and Exposition. March 14-18, 1993, Anaheim, California. For registration and additional information contact American College of Cardiology, 9111 Old Georgetown Rd, Bethesda, MD 20814-1699; (301) 897-5400, (800) 253-4636.

CARDIOVASCULAR CONFERENCE AT LAKE LOUISE. March 29-April 1, 1993. Lake Louise, Alberta, Canada. Fees: $410 for ACC members; $495 for non-members; $250 for residents, fellows-in-training, nurses, and technologists. 18.5 Category 1 credit hours. For information, call American College of Cardiology; (800) 257-4739, FAX (301) 897-9745.

CARDIOLOGY FIESTA IN SAN ANTONIO. April 22-24, 1993. Hyatt Regency San Antonio, Texas. Fees: $395 for ACC members; $465 for non-members; $250 for residents, fellows-in-training, physician assistants, nurses, and technologists. For information, call American College of Cardiology; (800) 257-4739, FAX (301) 897-9745.

CARDIOLOGY FOR THE PRIMARY PHYSICIAN during Spoleto Festival USA 1993, June 1-5, 1993. The Omni Hotel, Charleston, South Carolina. Fees: $410 for ACC members; $495 for non-members; $250 for residents, fellows-in-training, physician assistants, nurses, and technologists. For information, call American College of Cardiology; (800) 257-4739, FAX (301) 897-9745.

FELLOWSHIP

STD FELLOWSHIP. One year training program in clinical and epidemiological aspects of sexually transmitted diseases available July 1, 1993. Jointly sponsored by the University of California, San Francisco and San Francisco Department of Public Health. Send inquiries with CV to STD/P/T Center, 1360 Mission St, Ste 401, San Francisco, CA 94103, Attention Gail Bolan, MD. An EOE/AA Employer, M/F.

PRAVACHOL® (Pravastatin Sodium Tablets)

CONTRAINDICATIONS

Hypersensitivity to any component of this medication.

Active liver disease or unexplained, persistent elevations in liver function tests (see WARNINGS).

Pregnancy and lactation. Atherosclerosis is a chronic process and discontinuation of lipid-lowering drugs during pregnancy should have little impact on the outcome of long-term therapy of primary hypercholesterolemia. Cholesterol and other products of cholesterol biosynthesis are essential components for fetal development (including synthesis of steroids and cell membranes). Since HMG-CoA reductase inhibitors decrease cholesterol synthesis and possibly the synthesis of other biologically active substances derived from cholesterol, they may cause fetal harm when administered to pregnant women. Therefore, HMG-CoA reductase inhibitors are contraindicated during pregnancy and in nursing mothers. **Pravastatin should be administered to women of childbearing age only when such patients are highly unlikely to conceive and have been informed of the potential hazards.** If the patient becomes pregnant while taking this class of drug, therapy should be discontinued and the patient apprised of the potential hazard to the fetus.

WARNINGS

Liver Enzymes: HMG-CoA reductase inhibitors, like some other lipid-lowering therapies, have been associated with biochemical abnormalities of liver function. Increases of serum transaminase (ALT, AST) values to more than 3 times the upper limit of normal occurring on 2 or more (not necessarily sequential) occasions have been reported in 1.3% of patients treated with pravastatin in the U.S. over an average period of 18 months. These abnormalities were not associated with cholestasis and did not appear to be related to treatment duration. In those patients in whom these abnormalities were believed to be related to pravastatin and who were discontinued from therapy, the transaminase levels usually fell slowly to pretreatment levels. These biochemical findings are usually asymptomatic although worldwide experience indicates that anorexia, weakness, and/or abdominal pain may also be present in rare patients.

As with other lipid-lowering agents, liver function tests should be performed during therapy with pravastatin. Serum aminotransferases, including ALT (SGPT), should be monitored before treatment begins, every six weeks for the first three months, every eight weeks during the remainder of the first year, and periodically thereafter (e.g., at about six-month intervals). Special attention should be given to patients who develop increased transaminase levels. Liver function tests should be repeated to confirm an elevation and subsequently monitored at more frequent intervals. If increases in AST and ALT equal or exceed three times the upper limit of normal and persist, then therapy should be discontinued. Persistence of significant aminotransferase elevations following discontinuation of therapy may warrant consideration of liver biopsy.

Active liver disease or unexplained transaminase elevations are contraindications to the use of pravastatin (see CONTRAINDICATIONS). Caution should be exercised when pravastatin is administered to patients with a history of liver disease or heavy alcohol ingestion (see CLINICAL PHARMACOLOGY: Pharmacokinetics/Metabolism). Such patients should be closely monitored, started at the lower end of the recommended dosing range, and titrated to the desired therapeutic effect.

Skeletal Muscle: Rhabdomyolysis with renal dysfunction secondary to myoglobinuria has been reported with pravastatin and other drugs in this class. Uncomplicated myalgia has also been reported in pravastatin-treated patients (see ADVERSE REACTIONS). Myopathy, defined as muscle aching or muscle weakness in conjunction with increases in creatine phosphokinase (CPK) values to greater than 10 times the upper limit of normal was reported to be possibly due to pravastatin in only one patient in clinical trials (<0.1%). Myopathy should be considered in any patient with diffuse myalgias, muscle tenderness or weakness, and/or marked elevation of CPK. Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever. **Pravastatin therapy should be discontinued if markedly elevated CPK levels occur or myopathy is diagnosed or suspected. Pravastatin therapy should also be temporarily withheld in any patient experiencing an acute or serious condition predisposing to the development of renal failure secondary to rhabdomyolysis, e.g., sepsis; hypotension; major surgery; trauma; severe metabolic, endocrine, or electrolyte disorders; or uncontrolled epilepsy.**

The risk of myopathy during treatment with lovastatin is increased if therapy with either cyclosporine, gemfibrozil, erythromycin, or niacin is administered concurrently. There is no experience with the use of pravastatin together with cyclosporine. Myopathy has not been observed in clinical trials involving small numbers of patients who were treated with pravastatin together with niacin. One trial of limited size involving combined therapy with pravastatin and gemfibrozil showed a trend toward more frequent CPK elevations and patient withdrawals due to musculoskeletal symptoms in the group receiving combined treatment as compared with the groups receiving placebo, gemfibrozil, or pravastatin monotherapy. Myopathy was not reported in this trial (see PRECAUTIONS: Drug Interactions). One patient developed myopathy when clofibrate was added to a previously well tolerated regimen of pravastatin; the myopathy resolved when clofibrate therapy was stopped and pravastatin treatment continued. **The use of fibrates alone may occasionally be associated with myopathy. The combined use of pravastatin and fibrates should generally be avoided.**

PRECAUTIONS

General: Pravastatin may elevate creatine phosphokinase and transaminase levels (see ADVERSE REACTIONS). This should be considered in the differential diagnosis of chest pain in a patient on therapy with pravastatin.

Homozygous Familial Hypercholesterolemia. Pravastatin has not been evaluated in patients with rare homozygous familial hypercholesterolemia. In this group of patients, it has been reported that HMG-CoA reductase inhibitors are less effective because the patients lack functional LDL receptors.

Renal Insufficiency. A single 20 mg oral dose of pravastatin was administered to 24 patients with varying degrees of renal impairment (as determined by creatinine clearance). No effect was observed on the pharmacokinetics of pravastatin or its 3α-hydroxy isomeric metabolite (SQ 31,906). A small increase was seen in mean AUC values and half-life ($t_{1/2}$) for the inactive enzymatic ring hydroxylation metabolite (SQ 31,945). Given this small sample size, the dosage administered, and the degree of individual variability, patients with renal impairment who are receiving pravastatin should be closely monitored.

Information for Patients: Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever.

Drug Interactions: *Immunosuppressive Drugs, Gemfibrozil, Niacin (Nicotinic Acid), Erythromycin:* See WARNINGS: Skeletal Muscle.

Antipyrine: Clearance by the cytochrome P450 system was unaltered by concomitant administration of pravastatin. Since pravastatin does not appear to induce hepatic drug-metabolizing enzymes, it is not expected that any significant interaction of pravastatin with other drugs (e.g., phenytoin, quinidine) metabolized by the cytochrome P450 system will occur.

Cholestyramine/Colestipol: Concomitant administration resulted in an approximately 40 to 50% decrease in the mean AUC of pravastatin. However, when pravastatin was administered 1 hour before or 4 hours after cholestyramine or 1 hour before colestipol and a standard meal, there was no clinically significant decrease in bioavailability or therapeutic effect. (See DOSAGE AND ADMINISTRATION: Concomitant Therapy.)

Warfarin: In a study involving 10 healthy male subjects given pravastatin and warfarin concomitantly for 6 days, bioavailability parameters at steady state for pravastatin (parent compound) were not altered. Pravastatin did not alter the plasma protein-binding of warfarin. Concomitant dosing did increase the AUC and Cmax of warfarin but did not produce any changes in its anticoagulant action (i.e., no increase was seen in mean prothrombin time after 6 days of concomitant therapy). However, bleeding and extreme prolongation of prothrombin time has been reported with another drug in this class. Patients receiving warfarin-type anticoagulants should have their prothrombin times closely monitored when pravastatin is initiated or the dosage of pravastatin is changed.

Cimetidine: The $AUC_{0\text{-}12hr}$ for pravastatin when given with cimetidine was not significantly different from the AUC for pravastatin when given alone. A significant difference was observed between the AUC's for pravastatin when given with cimetidine compared to when administered with antacid.

Digoxin: In a crossover trial involving 18 healthy male subjects given pravastatin and digoxin concurrently for 9 days, the bioavailability parameters of digoxin were not affected. The AUC of pravastatin tended to increase, but the overall bioavailability of pravastatin plus its metabolites SQ 31,906 and SQ 31,945 was not altered.

Gemfibrozil: In a crossover study in 20 healthy male volunteers given concomitant single doses of pravastatin and gemfibrozil, there was a significant decrease in urinary excretion and protein binding of pravastatin. In addition, there was a significant increase in AUC, Cmax, and Tmax for the pravastatin metabolite SQ 31,906. Combination therapy with pravastatin and gemfibrozil is generally not recommended.

In interaction studies with *aspirin, antacids* (1 hour prior to PRAVACHOL), *cimetidine, nicotinic acid,* or *probucol,* no statistically significant differences in bioavailability were seen when PRAVACHOL (pravastatin sodium) was administered.

Other Drugs: During clinical trials, no noticeable drug interactions were reported when PRAVACHOL was added to: diuretics, antihypertensives, digitalis, converting-enzyme inhibitors, calcium channel blockers, beta-blockers, or nitroglycerin.

Endocrine Function: HMG-CoA reductase inhibitors interfere with cholesterol synthesis and lower circulating cholesterol levels and, as such, might theoretically blunt adrenal or gonadal steroid hormone production. Results of clinical trials with pravastatin in males and post-menopausal females were inconsistent with regard to possible effects of the drug on basal steroid hormone levels. In a study of 21 males, the mean testosterone response to human chorionic gonadotropin was significantly reduced ($p<0.004$) after 16 weeks of treatment with 40 mg of pravastatin. However, the percentage of patients showing a ≥50% rise in plasma testosterone after human chorionic gonadotropin stimulation did not change significantly after therapy in these patients. The effects of HMG-CoA reductase inhibitors on spermatogenesis and fertility have not been studied in adequate numbers of patients. The effects, if any, of pravastatin on the pituitary-gonadal axis in pre-menopausal females are unknown. Patients treated with pravastatin who display clinical evidence of endocrine dysfunction should be evaluated appropriately. Caution should also be exercised if an HMG-CoA reductase inhibitor or other agent used to lower cholesterol levels is administered to patients also receiving other drugs (e.g., ketoconazole, spironolactone, cimetidine) that may diminish the levels or activity of steroid hormones.

CNS Toxicity: CNS vascular lesions, characterized by perivascular hemorrhage and edema and mononuclear cell infiltration of perivascular spaces, were seen in dogs treated with pravastatin at a dose of 25 mg/kg/day, a dose that produced a plasma drug level about 50 times higher than the mean drug level in humans taking 40 mg/day. Similar CNS vascular lesions have been observed with several other drugs in this class.

A chemically similar drug in this class produced optic nerve degeneration (Wallerian degeneration of retinogeniculate fibers) in clinically normal dogs in a dose-dependent fashion starting at 60 mg/kg/day, a dose that produced mean plasma drug levels about 30 times higher than the mean drug level in humans taking the highest recommended dose (as measured by total enzyme inhibitory activity). This same drug also produced vestibulocochlear Wallerian-like degeneration and retinal ganglion cell chromatolysis in dogs treated for 14 weeks at 180 mg/kg/day, a dose which resulted in a mean plasma drug level similar to that seen with the 60 mg/kg dose.

Carcinogenesis, Mutagenesis, Impairment of Fertility: In a 2-year study in rats fed pravastatin at doses of 10, 30, or 100 mg/kg body weight, there was an increased incidence of hepatocellular carcinomas in males at the highest dose ($p<0.01$). Although rats were given up to 125 times the human dose (HD) on a mg/kg body weight basis, their serum drug levels were only 6 to 10 times higher than those measured in humans given 40 mg pravastatin as measured by AUC.

The oral administration of 10, 30, or 100 mg/kg (producing plasma drug levels approximately 0.5 to 5.0 times human drug levels at 40 mg) of pravastatin to mice for 22 months resulted in a statistically significant increase in the incidence of malignant lymphomas in treated females when all treatment groups were pooled and compared to controls ($p<0.05$). The incidence was not dose-related and male mice were not affected.

A chemically similar drug in this class was administered to mice for 72 weeks at 25, 100, and 400 mg/kg body weight, which resulted in mean serum drug levels approximately 3, 15, and 33 times higher than the mean human serum drug concentration (as total inhibitory activity) after a 40 mg oral dose. Liver carcinomas were significantly increased in high-dose females and mid- and high-dose males, with a maximum incidence of 90 percent in males. The incidence of adenomas of the liver was significantly increased in mid- and high-dose females. Drug treatment also significantly increased the incidence of lung adenomas in mid- and high-dose males and females. Adenomas of the eye Harderian gland (a gland of the eye of rodents) were significantly higher in high-dose mice than in controls.

No evidence of mutagenicity was observed *in vitro*, with or without rat-liver metabolic activation, in the following studies: microbial mutagen tests, using mutant strains of *Salmonella typhimurium* or *Escherichia coli*; a forward mutation assay in L5178Y TK +/− mouse lymphoma cells; a chromosomal aberration test in hamster cells; and a gene conversion assay using *Saccharomyces cerevisiae*. In addition, there was no evidence of mutagenicity in either a dominant lethal test in mice or a micronucleus test in mice.

In a study in rats, with daily doses up to 500 mg/kg, pravastatin did not produce any adverse effects on fertility or general reproductive performance. However, in a study with another HMG-CoA reductase inhibitor, there was decreased fertility in male rats treated for 34 weeks at 25 mg/kg body weight, although this effect was not observed in a subsequent fertility study when this same dose was administered for 11 weeks (the entire cycle of spermatogenesis, including epididymal maturation). In rats treated with this same reductase inhibitor at 180 mg/kg/day, seminiferous tubule degeneration (necrosis and loss of spermatogenic epithelium) was observed. Although not seen with pravastatin, two similar drugs in this class caused drug-related testicular atrophy, decreased spermatogenesis, spermatocytic degeneration, and giant cell formation in dogs. The clinical significance of these findings is unclear.

Pregnancy: Pregnancy Category X: See CONTRAINDICATIONS.

Safety in pregnant women has not been established. Pravastatin was not teratogenic in rats at doses up to 1000 mg/kg daily or in rabbits at doses of up to 50 mg/kg daily. These doses resulted in 20x (rabbit) or 240x (rat) the human exposure based on surface area ($mg/meter^2$). However, in studies with another HMG-CoA reductase inhibitor, skeletal malformations were observed in rats and mice. PRAVACHOL (pravastatin sodium) should be administered to women of child-bearing potential only when such patients are highly unlikely to conceive and have been informed of the potential hazards. If the woman becomes pregnant while taking PRAVACHOL (pravastatin sodium), it should be discontinued and the patient advised again as to the potential hazards to the fetus.

Nursing Mothers: A small amount of pravastatin is excreted in human breast milk. Because of the potential for serious adverse reactions in nursing infants, women taking PRAVACHOL should not nurse (see CONTRAINDICATIONS).

Pediatric Use: Safety and effectiveness in individuals less than 18 years old have not been established. Hence, treatment in patients less than 18 years old is not recommended at this time. (See also PRECAUTIONS: **General.**)

ADVERSE REACTIONS

Pravastatin is generally well tolerated; adverse reactions have usually been mild and transient. In 4-month long placebo-controlled trials, 1.7% of pravastatin-treated patients and 1.2% of placebo-treated patients were discontinued from treatment because of adverse experiences attributed to study drug therapy; this difference was not statistically significant. In long-term studies, the most common reasons for discontinuation were asymptomatic serum transaminase increases and mild, non-specific gastrointestinal complaints. During clinical trials the overall incidence of adverse events in the elderly was not different from the incidence observed in younger patients.

Adverse Clinical Events: All adverse clinical events (regardless of attribution) reported in more than 2% of pravastatin-treated patients in the placebo-controlled trials are identified in the table below; also shown are the percentages of patients in whom these medical events were believed to be related or possibly related to the study drug:

	All Events %		Events Attributed to Study Drug %	
Body System/Event	Pravastatin (N = 900)	Placebo (N = 411)	Pravastatin (N = 900)	Placebo (N = 411)
Cardiovascular				
Cardiac Chest Pain	4.0	3.4	0.1	0.0
Dermatologic				
Rash	4.0*	1.1	1.3	0.9
Gastrointestinal				
Nausea/Vomiting	7.3	7.1	2.9	3.4
Diarrhea	6.2	5.6	2.0	1.9
Abdominal Pain	5.4	6.9	2.0	3.9
Constipation	4.0	7.1	2.4	5.1
Flatulence	3.3	3.6	2.7	3.4
Heartburn	2.9	1.9	2.0	0.7
General				
Fatigue	3.8	3.4	1.9	1.0
Chest Pain	3.7	1.9	0.3	0.2
Influenza	2.4*	0.7	0.0	0.0
Musculoskeletal				
Localized Pain	10.0	9.0	1.4	1.5
Myalgia	2.7	1.0	0.6	0.0
Nervous System				
Headache	6.2	3.9	1.7*	0.2
Dizziness	3.3	3.2	1.0	0.5
Renal/Genitourinary				
Urinary Abnormality	2.4	2.9	0.7	1.2
Respiratory				
Common Cold	7.0	6.3	0.0	0.0
Rhinitis	4.0	4.1	0.1	0.0
Cough	2.6	1.7	0.1	0.0

*Statistically significantly different from placebo.

The following effects have been reported with drugs in this class:

Skeletal: myopathy, rhabdomyolysis.

Neurological: dysfunction of certain cranial nerves (including alteration of taste, impairment of extra-ocular movement, facial paresis), tremor, vertigo, memory loss, paresthesia, peripheral neuropathy, peripheral nerve palsy.

Hypersensitivity Reactions: An apparent hypersensitivity syndrome has been reported rarely which has included one or more of the following features: anaphylaxis, angioedema, lupus erythematous-like syndrome, polymyalgia rheumatica, vasculitis, purpura, thrombocytopenia, leukopenia, hemolytic anemia, positive ANA, ESR increase, arthritis, arthralgia, urticaria, asthenia, photosensitivity, fever, chills, flushing, malaise, dyspnea, toxic epidermal necrolysis, erythema multiforme, including Stevens-Johnson syndrome.

Gastrointestinal: pancreatitis, hepatitis, including chronic active hepatitis, cholestatic jaundice, fatty change in liver, and, rarely, cirrhosis, fulminant hepatic necrosis, and hepatoma; anorexia, vomiting.

Reproductive: gynecomastia, loss of libido, erectile dysfunction.

Eye: progression of cataracts (lens opacities), ophthalmoplegia.

Laboratory Test Abnormalities: Increases in serum transaminase (ALT, AST) values and CPK have been observed (see WARNINGS).

Transient, asymptomatic eosinophilia has been reported. Eosinophil counts usually returned to normal despite continued therapy. Anemia, thrombocytopenia, and leukopenia have been reported with other HMG-CoA reductase inhibitors.

Concomitant Therapy: Pravastatin has been administered concurrently with cholestyramine, colestipol, nicotinic acid, probucol and gemfibrozil. Preliminary data suggest that the addition of either probucol or gemfibrozil to therapy with lovastatin or pravastatin is **not** associated with greater reduction in LDL-cholesterol than that achieved with lovastatin or pravastatin alone. No adverse reactions unique to the combination or in addition to those previously reported for each drug alone have been reported. Myopathy and rhabdomyolysis (with or without acute renal failure) have been reported when another HMG-CoA reductase inhibitor was used in combination with immunosuppressive drugs, gemfibrozil, erythromycin, or lipid-lowering doses of nicotinic acid. Concomitant therapy with HMG-CoA reductase inhibitors and these agents is generally not recommended. (See WARNINGS: **Skeletal Muscle** and PRECAUTIONS: **Drug Interactions.**)

OVERDOSAGE

There have been no reports of overdoses with pravastatin.

Should an accidental overdose occur, treat symptomatically and institute supportive measures as required.

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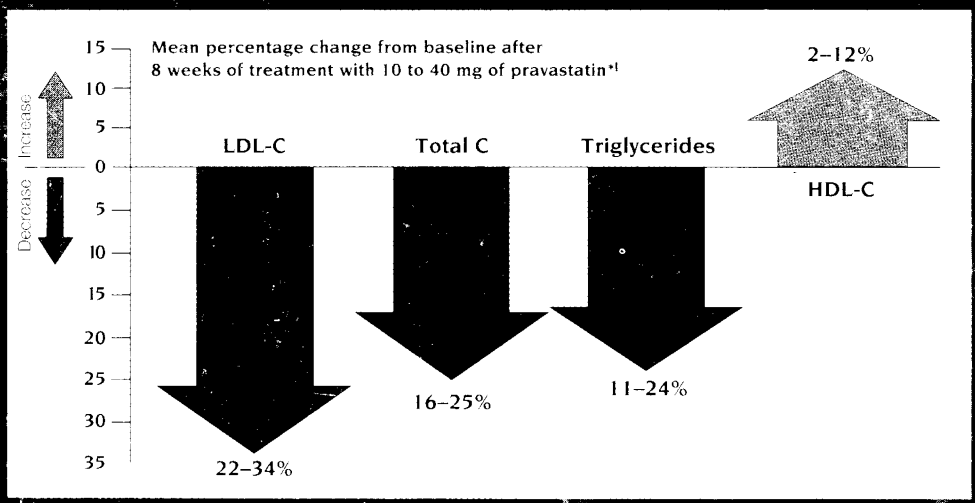
Bristol-Myers Squibb Company

Effective cholesterol control

Consistently and significantly reduces total C and atherogenic LDL-C; positively affects other key lipids



*Each arrow represents a range of means derived from a single placebo-controlled study that included 55 patients treated with pravastatin.

PRAVACHOL® (pravastatin sodium) is indicated as an adjunct to diet for the reduction of elevated total and LDL-cholesterol levels in patients with primary hypercholesterolemia (Types IIa and IIb) when the response to diet alone has not been adequate.

Active liver disease *or* unexplained transaminase elevations, pregnancy and lactation are contraindications to the use of pravastatin.

Reference: 1. Jones PH, et al. Once-daily pravastatin in patients with primary hypercholesterolemia: a dose-response study. *Clin Cardiol.* 1991;14:146-151.

PRAVACHOL™

pravastatin sodium 20 mg tablets

Please see CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS in the brief summary of prescribing information on the adjacent page.

Bristol-Myers Squibb Company